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Application Number	09/976,423
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First Named Inventor	Kirk Hogan
Art Unit	1634
Examiner Name	J.A. Goldberg
Attorney Docket Number	HOGAN-06650

ENCLOSURES *(Check all that apply)*

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment/Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Reply to Missing Parts/ Incomplete Application
  - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
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- ☒ Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
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- ☐ Other Enclosure(s) (please Identify below):

Remarks

Appellant's herewith file Appellant's Reply Brief in triplicate.

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	MEDLEN & CARROLL, LLP		
Signature			
Printed name	David A. Casimir		
Date	February 28, 2006	Reg. No.	42,395

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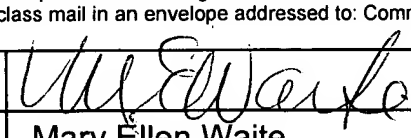
Signature			
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Kirk Hogan		
Serial No.:	09/976,423	Group No.:	1634
Filed:	10/21/2001	Examiner:	J.A. Goldberg
Entitled:	**Methods and Compositions for Perioperative Genomic Profiling**		

APPELLANT'S REPLY BRIEF

APPEAL NO.:

CERTIFICATE OF FACSIMILE TRANSMISSION UNDER 37 C.F.R. § 1.8(a)(1)(i)(B)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Appeal Brief – Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313 1450.

Dated: February 28, 2006

By: Mary Ellen Waite

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Madam/Sir:

This Reply is in reply to the Examiner's Answer Mailed December 30, 2005, to the Appellant's Brief, filed November 9, 2005.

It is not believed that any fees are necessary for this reply. However, if any fees are necessary, the Examiner is hereby authorized to charge Deposit Account No. 08-1290 the fee associated with this Reply Brief and any other fees associated with this communication. Please reference Attorney Docket No.: HOGAN-06650 when charging the Attorney Deposit Account.

This Brief is transmitted in triplicate. [37 CFR § 1.192(a).]

I. STATUS OF CLAIMS

Claims 1-23 were filed in the original application. During prosecution of the application, Claims 1-23 were cancelled and Claims 24-44 were added in the Amendment and Response to Office Action filed January 8, 2003. Claims 24-44 were cancelled and Claims 45-71 were added in the Amendment and Response to Office Action filed May 23, 2003. Claims 69 and 70 were cancelled in the Amendment and Response to Final Office Action filed June 30, 2004. Claims 45-68, and 71 were cancelled, and Claims 72-107 were added in the Amendment and Response to Office Action filed February 14, 2005. Claims 72-107 have been rejected by the Office in the Final Office Action dated May 10, 2005. No other Claims are pending. Therefore, Claims 72-107 are pending in this appeal. The Appellant appeals the Final Office Action of May 10, 2005.

The Claims, as they now stand, are set forth in APPENDIX A: PENDING CLAIMS.

II. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

There are two old grounds of rejection to be reviewed in the original brief, and three new grounds of rejection introduced in the Examiner's Answer:

Ground of Rejection 1 – Whether Claims 72-107 contain subject matter that was not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor at the time the application was filed, had possession of the claimed invention; and

Ground of Rejection 2 – Whether Claims 72-107 are anticipated by the 1993 Applied Biosystems Product Catalog, pages 135-164.

The Appellant presented Claims 106-107 in the Amendment and Response to Office Action of August 24, 2004 (mailed February 14, 2005) and, as pointed out in the Appellant's Brief, while Claims 106-107 were entered, they were not examined in the Final Office Action (mailed May 10, 2005).

In the Examiner's Answer of December 30, 2005 the Examiner's Answer subsequently adds three new rejections:

New Ground of Rejection 3 – Whether Claims 106-107 are anticipated by the Perkin Elmer, PCR Systems, Reagents & Consumables catalog (1995-1996, pages 15-18) (hereinafter "Perkin Elmer").

New Ground of Rejection 4 – Whether Claims 106-107 are obvious over Rosen (U.S. Publication 2002/0119468, August, 2002) (hereinafter "Rosen") in view of Ahern (The Scientist, Vol 9, No. 15, page 20, July, 1995) (hereinafter "Ahern").

New Ground of Rejection 5 – Whether Claims 106-107 are obvious over Tarkowski *et al.* (Neurology, Vol 54, pages 2077-2081, June 13, 2000) (hereinafter "Tarkowski") in view of Ahern.

III. ARGUMENT

A. Ground of Rejection 1 - The Specification Fully Supports the Subject Matter of Claims 72-105

The present invention claims kits for generating a perioperative genomic profile for a subject undergoing surgery comprising reagents sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the list consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*, and a computer program comprising instructions which direct a processor to analyze data derived for use of the reagents. As pointed out to the Examiner (Appellant's Brief, page 15), the proper legal standard is clear *i.e.*, the Specification "'must simply indicate to persons skilled in the art that as of the [filing] date the applicant had invented what is now claimed.' *Eiselstein v. Frank*, F.3d 1035, 1038, 34 USPQ2d 1467, 1470 (Fed. Cir. 1995) (citing *Vas-Cath*, 935 F.2d at 1562, 19 USPQ2d at 1115, and *In re Wertheim*, 541 F.2d 257, 265, 191 U.S.P.Q. 90, 98 (CCPA 19769)."[1] While the Examiner's Answer expressly acknowledges this standard ("The Appellant correctly asserts that adequate description under 112, first paragraph does not require verbatim support, however the recitation must be conveyed to the skilled artisan.", page 15), the Examiner ignores its authority.

For example, the Examiner's Answer declares "The brief fails to ever provide a passage that supports a computer program in a kit with reagents." (Examiner's Answer, page 15). To the contrary, the Appellant's Brief (pages 13-21) points to multiple, explicit support for the claims to be found in the Specification, for example: "In some embodiments (*i.e.*, embodiments of the kits of the present invention), a computer-based analysis program is used to translate raw data generated by the genomic profile (e.g., the presence or absence of a given SNP or mutation) into data of predictive value for the clinician (e.g., a probability of abnormal pharmacological response, presence of an underlying disease, or differential diagnosis of known disease). (Specification, page 50,

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[1] *All Dental Prodx, LLC v. Advantage Dental Products, Inc.*, 309 F.3d 774, 64 USPQ2d, 1945 (Fed. Cir. 2002).

lines 8 – 12.) (Emphasis added.) And, for example, **Section II. "Assays for Generating Genomic Profiles", Subsection E. "Computerized Data Analysis"** (Specification, page 49, lines 4-12). The Examiner's Answer argues that the Specification fails to reasonably convey the claimed subject matter to an artisan of ordinary skill, but then the Examiner explicitly concedes "the brief points to numerous passages and numerous recitations of computer programs." (Examiner's Answer, page 16). (Emphasis added). The Appellant reminds the Examiner that the claim elements in question (*e.g.*, computer programs), and explicit support in the Specification (as acknowledged by the Examiner's Answer), are joined in the present invention by design and intent to thereby arrive at the present invention and not, as the Examiner impugns, by chance or by whim.

In addition to explicit and literal support, one skilled in the art would appreciate from the context provided by the Specification numerous additional aspects of the kits and computer programs of the present invention. For example, **Section III. Analysis and Delivery of Data** (pages 49 – 53) describes implementation of software for data collection, analysis and presentation. One skilled in the art would appreciate that all such methods may be applied to kits in view of the Appellant's statements that the kits of the present invention can include software for analyzing data.

B. Ground of Rejection 2 - Claims 72-107 Are Not Anticipated by the 1993 Applied Biosystems Product Catalog, pages 135-164.

1. The Examiner's Reference Does Not Teach All Claim Elements

The Examiner's Answer argues: "The Appellant asserts that the prior art does not teach the specific variant allele elements of the present claims because Applied Biosystems does not teach "reagents sufficient to detect the presence or absence of variant alleles" and the reference doe not mention the genes recited in the claims (see page 24 of Brief). This argument has been reviewed but is not convincing because the claims recite "reagents which detect the presence of variant alleles in two or more genes.

. . " This limitation does not require any allele specific elements." (Examiner's Answer, page 16). (Emphasis added).

To the contrary, and as pointed out to the Examiner in the Appellant's Brief (page 26), Claim 72 actually reads: "reagents configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*." (Emphasis added). If this limitation does not require allele specific elements (as the Examiner alleges), then how are the variant alleles in the specified genes to be detected as expressly claimed?

Surprisingly, the Examiner, persistently and without explanation, ignores limitations (underscored above) that provide the allele specific elements that the Examiner argues are not there. Nor does the Examiner's Answer indicate where these elements are to be found in the 1993 Applied Biosystems Product Catalog, or respond to the Appellant's exhibit of these deficiencies in the Examiner's arguments. (Appellant's Brief, page 26). Instead, the Examiner argues "If the sequence is sequenced using the analysis system and the other reagents taught by Applied Biosystems, the ordinary artisan would have determined the presence or absence of a variant allele, for example." (Examiner's Answer, page 17). The Examiner's Answer is wrong with regard to the facts of both the cited reference, and the present invention. The Applied Biosystems Catalog does not teach reagents "sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*." lacking, for example, any instruction that would direct the artisan to these genes or to these variant alleles, any motivation to target these genes, or any reagents (*e.g.*, primer sequences) sufficient for detecting the presence or absence of the recited alleles.

The Examiner's rejection impermissibly rests on the Examiner's truncated edition of the claims, and not the actual claims in pendency. As well, the Examiner's Answer represents a gross over-reading of the Applied Biosystems Catalog. Hence, the Examiner

sees elements in the Applied Biosystems Catalog that are not there, and ignores elements in claims of the present invention in plain sight.

2. *In re Ngai* Stands for the Patentability of Claims 72-105

The Examiner's Answer argues "Additionally, in view of the recent Federal Circuit case holding that an inventor could not patent known kits simply by attaching new sets of instructions to that product (sic). See In re Ngai, 367 F.3d 1336, 70 U.S.P.Q. 2d 1862 (Fed. Cir. 2004). This is the precise issue argued at length by the instant response (pages 30-34). Since the facts and analysis of the instant application are analogous, Ngai is deemed the closest authority on the issue of whether printed instructions in a previously disclosed kit makes the kit patentable." (Examiner's Answer, page 18).

In this misreading of Ngai the Examiner makes a number of errors. First, the kits of the present invention are not "previously disclosed". As detailed above, and in the Appellant's Brief (pages 22-30), the Examiner's cited reference (the Applied Biosystems Catalog) lacks not one, or several, but multiple express elements of the claims. Nevertheless, the Examiner proceeds to edit out still further elements of the claims. For example, the Examiner argues "This argument has been thoroughly reviewed, but is not found persuasive because the kit is not previously unknown. The kit is merely reagents which are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα and TNFβ so as to generate a genomic profile." (Examiner's Answer, page 19). (Emphasis added). The Appellant appreciates that the Examiner chooses (for once) to acknowledge these elements of the claims, and to recite them in their entirety, however in so doing the Examiner edits out yet another element *en bloc*, *e.g.*, "b) a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents." (Claim 72). Clearly, the kit is not "merely reagents." Only by ignoring one element after another is the Examiner able to make the unsupported and erroneous assertion that "the kit is merely reagents", or that the kits of the present invention are previously known.

Second, the Examiner's Answer perseveres in confusing the printed matter instructions of *In re Ngai* with a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents of the present claims. As pointed out to the Examiner in the Appellant's Brief "Contrary to the Examiner's misinterpretation, *In re Ngai* does not address, consider or even mention computers, computer programs, computer programs comprising instructions, or computer analysis of data." (Appellant's Brief, page 37) (Emphasis in original). The Examiner's Answer is silent with regard to these defects of *In re Ngai*.

Moreover, the Examiner's selective vision extends to the MPEP itself. The Examiner argues "Further, as noted above, its is clear from the MPEP that data or instructions on a computer program is deemed to be non-functional descriptive matter." (Examiner's Answer, page 21). The Examiner is in error. Contrary to the Examiner's selective reading, the MPEP explains: "Descriptive material can be characterized as "functional descriptive material" or "non-functional descriptive material." In this context, "functional descriptive material" consists of data structures and computer programs which impart functionality when employed as a computer component. (The definition of "data structure" is "a physical or logical relationship among data elements, designed to support specific data manipulation functions.) . . . "Nonfunctional descriptive material" includes, but is not limited to music, literary works and a compilation or mere arrangement of data." (MPEP 2100-11 – 2100-12). As pointed out to the Examiner (Appellant's Brief, page 38), computer instructions which direct a processor to analyze data for generating a perioperative genomic profile for a subject as claimed, qualify as statutory subject matter because storage of the computer instructions turns a computer readable medium into a functional component which directly cooperates with the processor. Computer instructions cause computer functions to occur, and are therefore inarguably functional components of the computer system. These facts are uncontested in the Examiner's Answer. In turn, the Examiner argues "It is noted that the instant computer program is not embodied on a tangible medium, for example, as required by Beauregard." (Examiner's Answer, page 21). This observation is directly negated by the Examiner's own acknowledgement that the computer program comprising instructions which direct a processor (*i.e.*, a "tangible medium") of the present invention are

"instructions printed in the memory of the computer for execution" (*i.e.*, on a tangible medium). (Final Office Action, May 19, 2005, page 7).

Finally, the Examiner speculates "To allow Appellant to "write" their "instructions" on a computer program rather than on a piece of paper would not appear to be in accordance with the substance of the opinion provided in Ngai." (Examiner's Answer, page 21). Once again the Examiner misinterprets the claims and the law. The computer program of the claims does not simply display written instructions to a user of reagents as the Examiner suggests in an attempt to apply the Ngai case.[2] In contrast, the computer program of the present invention instructs a processor to analyze data, *i.e.*, a classically patentable use of a computer programs.[3] The Appellant notes that even if the computer program simply displayed instructions to a user of the reagents, it is still patentable subject matter for the reasons of record (see Declaration of Morris Waxler, Ph.D., and associated discussion). The kits of the present invention are clearly not anticipated by the Examiner's citation of the Applied Biosystems Catalog. As well, Ngai never addresses computers or computer programs. Nor has the Examiner has ever put forward evidence or reasoning to dispute the functional relationships between the claimed computer-based instructions and other components of Claims 72-105.

C. Claims 106-107 Are Allowable and Have Not Been Examined

The Examiner improperly failed to review Claims 106 and 107 during original prosecution. To make up for this oversight the Examiner introduces new rejections for the first time during the present Answer on appeal. Remarkably, even these rejections blatantly fail to examine Claims 106 and 107. Instead, the Examiner's rejections are simply copy/pasted language relating to elements not even found in Claims 106 and 107.

In the Examiner's Answer of December 30, 2005, the Examiner has rejected Claims 106-107 35 U.S.C. 102(b) as being anticipated by the Perkin Elmer Catalog.

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[2] *In re Ngai*, 367 F.3d 1336, 70 U.S.P.Q. 2d 1862 (Fed. Cir. 2004)
[3] *Alappat*, 33 F.3d 1543, 31 USPQ2d 1556-1557 (quoting *Diamond v. Diehr*, 450 U.S., 192, 209 USPQ, 10), and *Diamond v. Diehr*, 450 U.S., 192, 209 USPQ, 6.

The Appellant observes that the Examiner's rejections have apparently been cut and pasted from an earlier Office Action, and the Examiner has not actually read, let alone examined, Claims 106 and 107.

For example, the Examiner's Answer argues "This argument has been reviewed but is not convincing because the claims recite "reagents which detect the presence of variant alleles of two or more genes ... This limitation does not require any specific elements. Reagents which detect the presence of variant alleles encompass any product which may enable detection of variant alleles. The specification, nor the instant claims, (sic) limits reagents to be nucleic acid or more specifically a nucleic acid flanking, or comprising a variant. . . . Rather the claim broadly encompasses ANY "reagents capable of detecting the presence of variant alleles of two or more genes ..." (Examiner's Answer, page 23) (Emphasis added).

The Examiner is in error. The element "reagents" appears nowhere in Claim 106 or Claim 107, nor does the limitation "reagents capable of detecting". Either the Examiner has impermissibly rewritten the claims, or the Examiner has not even read the claims.

As well, the Examiner's Answer argues: "With response to instructions, the response traverses the rejection (page 12, of response filed June 3, 2004)" (Examiner's Answer, page 23); and "Additionally, in view of the recent Federal Circuit case holding that an inventor could not patent known kits simply by attaching new sets of instructions to that product." (Examiner's Answer, page 24) (Emphasis added); and "Ngai is deemed the closest authority on the issue of whether printed instructions in a previously disclosed kit makes the kit patentable." (Examiner's Answer, page 24). (Emphasis added).

The Examiner is in error. The element "instructions" appears nowhere in Claim 106 or Claim 107. Either the Examiner has impermissibly rewritten the claims to add elements not provided by the inventor, or the Examiner has not even read the claims

Because the Examiner has failed again to examine Claims 106-107, the arguments of the Examiner's Answer are manifestly invalid, and the rejections must be withdrawn. Nevertheless, and while under no obligation to do so, the Appellant sets forth further deficiencies in the Examiner's Answer below.

1. New Ground of Rejection 3 – Claims 106 and 107 Are Not Anticipated by The Perkin Elmer Catalog

The text of 35 U.S.C. 102 (b) reads:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application in the United States.

The Appellant respectfully asserts that the Perkin Elmer Catalog reference cited by the Examiner glaringly fails to meet this standard of anticipation. To the contrary, the catalog pages do not teach a perioperative genomic profile kit. The catalog pages do not teach kits with component parts configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*. The Examiner's prior art reference does not provide a subject-specific clinical pathway for a subject. The Examiner's reference does not teach kits comprising information to optimize perioperative care that, based at least on the presence or absence of said variant alleles of two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*, direct a user to a specific clinical pathway. The Perkin Elmer Catalog does not teach a kit comprising information that directs a specific clinical pathway of medical intervention for a subject (Claim 106). The Perkin Elmer Catalog does not teach a kit comprising information that directs a specific clinical pathway of anesthesia intervention for a subject (Claim 107).

In the Examiner's Answer of December 30, 2005, the Examiner perseverates in re-asserting a rejection under 35 U.S.C. 102(b) only by improperly ignoring the absence

of these limitations in the Perkin Elmer Catalog cited as prior art reference. The Federal Circuit has stated the relevant analysis for anticipation as follows:

> "A claim is anticipated only if each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference."[4]

The Appellant respectfully submits that the Perkin Elmer Catalog cited by the Examiner fails to teach each and every element as set forth in the claims. The catalog pages cited by the Examiner have no teaching or suggestion to use variant alleles of two or more of the claimed genes in the claimed manner (or in any manner). Thus, none of the cited references teach or suggest kits having component parts configured to detect the specific variant alleles as recited in the claims.

In view of the above, the Appellant requests the Board withdraw this rejection of Claims 106 and 107.

2. New Ground of Rejection 4 – Claims 106 and 107 Are Not Obvious Over the Combination of Rosen and Ahern

A *prima facie* case of obviousness requires the Examiner to cite to a reference which a) discloses all the elements of the claimed invention, b) suggests or motivates one of ordinary skill in the art to combine the claim elements to yield the claimed invention, and c) provides a reasonable expectation of success should the claimed combination be carried out. Failure to establish any one of these three requirements negates a finding of a *prima facie* case and, without more, entitles the Applicants to allowance of the claims in issue. (MPEP)

a. The Examiner's Combinations of References Do Not Teach All Elements of The Claims

In the Examiner's Answer of December 30, 2005 the Examiner argues "the claims

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[4] *Verdegaal Bros. V. Union Oil of California*, 2 USPQ2d 1051, 1053 (Fed.Cir. 1987)

require reagents sufficient to detect variant alleles from TNFalpha and TNFbeta." (page 25). The Examiner is in error. To the contrary, the Appellants Claims 106 and 107 do not require "reagents".

Moreover, Rosen plus Ahern does not teach or suggest two or more genes associated with two or more conditions. Rosen plus Ahern does not teach or suggest kits providing "a subject-specific clinical pathway comprising information to optimize perioperative care." Rosen plus Ahern does not teach a specific clinical pathway of medical intervention for a perioperative subject (Claim 106), or a specific clinical pathway of anesthesia intervention for a perioperative subject (Claims 107).

Thus, the Examiner's combination fails to teach every element of the presently claimed invention and, without more, the Examiner is unable to sustain a *prima facie* case of obviousness. In view of the above, the Appellant respectfully requests that the rejection be withdrawn.

b. The Examiner's References Do Not Provide a Suggestion or Motivation to Combine the Recited Elements

An essential requirement for a *prima facie* case of obviousness is whether a person of ordinary skill in the art would be motivated to modify the reference to arrive at the claimed invention. The Appellant asserts that the Examiner has not met the burden of establishing a *prima facie* case of obviousness. *Prima facie* obviousness based on a combination of references requires that the prior art provide "a reason, suggestion, or motivation to lead an inventor to combine those references."[5] "The range of sources available, however, does not diminish the requirement for actual evidence. That is, the showing must be clear and particular. Broad conclusory statements regarding the teaching of multiple references, standing alone, are not "evidence"."[6] The suggestion to combine prior art references must come from the cited references, not from the Appellant's disclosure.[7]

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5 *Pro-Mold and Tool Co. v. Great Lakes Plastics Inc.*, 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

6 *In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999).

7 *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1998)

As set forth in *In re Kotzab*, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000):

> "A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. . . . Close adherence to this methodology is especially important in cases where the very ease with which the invention can be understood may prompt one "to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher."
>
> Most if not all inventions arise from a combination of old elements. . . . Thus, every element of a claimed invention may often be found in the prior art. . . . However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. . . . Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant."

The Examiner's rejection does not establish the requisite suggestion in the art to combine elements disclosed in the prior art. "A rejection cannot be predicated on the mere identification . . . of individual components of claimed limitations. Rather, particular findings must be made as to the reasons the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed."[8] The need for a specific suggestion in the cited references is absolute: "The factual inquiry whether to combine references must be thorough and searching. It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions and cannot be dispensed with."[9]

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[8] *Ecolochem*, 227 F.3d, 1361, 1375, 56 USPQ2d 1065, 1076, quoting *Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317.

[9] *In Re Sang Su Lee*, 277 F.3d 1338, 1341, USPQ2d 1430, 1433. (Fed. Cir. 2002).

Contrary to legal requirement, the Examiner's conclusory and unsupported assertion in the Examiner's Answer (page 26) regarding the motivation of an ordinary artisan in view of Rosen plus Ahern is not evidence. The Examiner does not, and cannot, point to which specific teachings in Rosen plus Ahern motivate the ordinary artisan to combine the claimed elements thereby arriving at the perioperative genomic profile kits of the present invention. Rather, the Examiner's assertion reflects the absence of evidence, and thus does not fulfill the obligation of the Patent and Trademark Office. The Examiner's Answer argues "In this case, Ahern teaches kits save time and money because kits already comes (sic) prepared. . . . Therefore, to place reagents for carrying out a method into a kit would have been obvious at the time the invention was made." (page 26). In *In re Saung Su Lee* the Court of Appeals for the Federal Circuit expressly prohibits this kind of substitution of the benefits of an invention for objective evidence of an invention's obviousness by the Patent and Trademark Office.[10]

Because the Examiner has failed to establish motivation to modify Rosen plus Ahern to arrive at the claimed invention, a *prima facie* case of obviousness must fail. In view of the above, the Appellant respectfully requests that the rejection be withdrawn.

c. The Examiner's Combinations of References Do Not Provide a Reasonable Expectation of Success

The Examiner's combinations are not sufficient for a reasonable expectation of success. Alone, or in combination Rosen plus Ahern provides no specific guidance, general guidance, or any guidance whatsoever in selecting component parts configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*, so as to generate a genomic profile for use in selecting a perioperative course of action for said subject and thereby providing a subject-specific clinical pathway

[10] *Ibid.*.

for said subject, comprising information to optimize perioperative care that, based at least on the presence or absence of said variant alleles of two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ* measured by said kit, directs a user to a specific clinical pathway of medical intervention or anesthesia intervention for said subject. Therefore, the Examiner cannot advance any evidence in support of the contention that the artisan using the methods of Rosen plus Ahern would have had a reasonable expectation of success. Because the Examiner is not able to show that a reasonable expectation of success may be found in Rosen plus Ahern, the third prong of a *prima facie* case of obviousness is defective, as are prongs one and two.

To the contrary, the Examiner has failed to establish not one, but all three of the requirements for a *prima facie* case of obviousness, thus entitling the Appellant to withdrawal of this rejection.

3. New Ground of Rejection 5 – Claims 106 and 107 Are Not Obvious Over the Combination of Tarkowski and Ahern

A *prima facie* case of obviousness requires the Examiner to cite to a reference which a) discloses all the elements of the claimed invention, b) suggests or motivates one of ordinary skill in the art to combine the claim elements to yield the claimed invention, and c) provides a reasonable expectation of success should the claimed combination be carried out. Failure to establish any one of these three requirements negates a finding of a *prima facie* case and, without more, entitles the Applicants to allowance of the claims in issue. (MPEP)

a. The Examiner's Combinations of References Do Not Teach All Elements of The Claims

In the Examiner's Answer of December 30, 2005 the Examiner argues "the claims require reagents sufficient to detect variant alleles from TNFalpha and TNFbeta." (page 26). (Emphasis added). The Examiner is in error. To the contrary, the claims do not require "reagents".

Moreover, Tarkowski plus Ahern does not teach or suggest two or more genes associated with two or more conditions. Tarkowski plus Ahern does not teach or suggest kits providing "a subject-specific clinical pathway comprising information to optimize perioperative care." Tarkowski plus Ahern does not teach a specific clinical pathway of medical intervention for a perioperative subject (Claim 106), or a specific clinical pathway of anesthesia intervention for a perioperative subject (Claims 107).

Thus, the Examiner's combinations fail to teach every element of the presently claimed invention and, without more, the Examiner is unable to sustain a *prima facie* case of obviousness. In view of the above, the Appellant respectfully requests that the rejection be withdrawn.

b. The Examiner's References Do Not Provide a Suggestion or Motivation to Combine the Recited Elements

An essential requirement for a *prima facie* case of obviousness is whether a person of ordinary skill in the art would be motivated to modify the reference to arrive at the claimed invention. The Appellant asserts that the Examiner has not met the burden of establishing a *prima facie* case of obviousness. *Prima facie* obviousness based on a combination of references requires that the prior art provide "a reason, suggestion, or motivation to lead an inventor to combine those references."[11] "The range of sources available, however, does not diminish the requirement for actual evidence. That is, the showing must be clear and particular. Broad conclusory statements regarding the teaching of multiple references, standing alone, are not "evidence"."[12] The suggestion to combine prior art references must come from the cited references, not from the applicant's disclosure.[13]

As set forth in *In re Kotzab*, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000):

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11 *Pro-Mold and Tool Co. v. Great Lakes Plastics Inc.*, 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

12 *In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999).

13 *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1998)

> "A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. . . . Close adherence to this methodology is especially important in cases where the very ease with which the invention can be understood may prompt one "to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher."
>
> Most if not all inventions arise from a combination of old elements. . . . Thus, every element of a claimed invention may often be found in the prior art. . . . However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. . . . Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant."

The Examiner's rejection does not establish the requisite suggestion in the art to combine elements disclosed in the prior art. "A rejection cannot be predicated on the mere identification . . . of individual components of claimed limitations. Rather, particular findings must be made as to the reasons the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed."[14] The need for a specific suggestion in the cited references is absolute: "The factual inquiry whether to combine references must be thorough and searching. It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions and cannot be dispensed with."[15]

Contrary to legal requirement, the Examiner's conclusory and unsupported assertion in the Examiner's Answer (page 27) regarding the motivation of an ordinary artisan in view of Tarkowski plus Ahern is not evidence. The Examiner does not, and cannot, point to which specific teachings in Tarkokowsi plus Ahern motivate the ordinary

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[14] *Ecolochem*, 227 F.3d, 1361, 1375, 56 USPQ2d 1065, 1076, quoting *Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317.

[15] *In Re Sang Su Lee*, 277 F.3d 1338, 1341, USPQ2d 1430, 1433. (Fed. Cir. 2002).

artisan to combine the claimed elements thereby arriving at the perioperative genomic profile kits of the present invention. Rather, the Examiner's assertion reflects the absence of evidence, and thus does not fulfill the obligation of the Patent and Trademark Office. The Examiner's Answer argues "In this case, Ahern teaches kits save time and money because kits already comes (sic) prepared. . . . Therefore, to place reagents for carrying out a method into a kit would have been obvious at the time the invention was made." (page 26). In *In re Saung Su Lee* the Court of Appeals for the Federal Circuit expressly prohibits this kind of substitution of the benefits of an invention for objective evidence of an invention's obviousness by the Patent and Trademark Office.[16]

Because the Examiner has failed to establish motivation to modify Tarkowski plus Ahern to arrive at the claimed invention, a *prima facie* case of obviousness must fail. In view of the above, the Appellant respectfully requests that the rejection be withdrawn.

c. The Examiner's Combinations of References Do Not Provide a Reasonable Expectation of Success

The Examiner's combinations are not sufficient for a reasonable expectation of success. Alone, or in combination Tarkowski plus Ahern provides no specific guidance, general guidance, or any guidance whatsoever in selecting component parts configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*, so as to generate a genomic profile for use in selecting a perioperative course of action for said subject and thereby providing a subject-specific clinical pathway for said subject, comprising information to optimize perioperative care that, based at least on the presence or absence of said variant alleles of two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ* measured by said kit, directs a

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[16] *Ibid.*

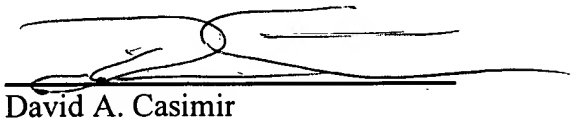
user to a specific clinical pathway of medical intervention or anesthesia intervention for said subject. Therefore, the Examiner cannot advance any evidence in support of the contention that the artisan using the methods of Tarkowski plus Ahern would have had a reasonable expectation of success. Because the Examiner is not able to show that a reasonable expectation of success may be found in Tarkowski plus Ahern, the third prong of a *prima facie* case of obviousness is defective, as are prongs one and two.

To the contrary, the Examiner has failed to establish not one, but all three of the requirements for a *prima facie* case of obviousness, thus entitling the Appellant to withdrawal of this rejection.

IV. CONCLUSION

For the foregoing reasons, it is submitted that the Examiner's rejection of Claims 72-107 was erroneous, and reversal of the rejection is respectfully requested. The Appellant requests that the Board render a decision as to the allowability of the Claims.

Dated: February 28, 2006



David A. Casimir
Registration No. 42,395

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
(608) 218-6900

APPENDIX A

PENDING CLAIMS

Claims 1 - 71 (cancelled).

72. (previously presented) A kit for generating a perioperative genomic profile for a subject, comprising:

a) reagents configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNF*α and *TNF*β so as to generate a genomic profile for use in selecting a perioperative course of action for said subject; and

b) a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents.

73. (previously presented) The kit of claim 72, wherein said instructions translate said data into information of predictive value for a clinician.

74. (previously presented) The kit of claim 72, wherein said instructions translate said data into a risk assessment for treatment options.

75. (previously presented) The kit of claim 72, wherein said instructions translate said data into recommendations for treatment options.

76. (previously presented) The kit of claim 72, wherein said instructions generate a report for display to a clinician.

77. (previously presented) The kit of claim 76, wherein said display is in the form of a report that can be printed.

78. (previously presented) The kit of claim 76, wherein said display is in the form of a report on a computer monitor.

79. (previously presented) The kit of claim 72, wherein said instructions are sufficient to receive, process and transmit said data to and from said subject, a clinical laboratory and medical personnel.

80. (previously presented) The kit of claim 73 wherein said transmission of said data uses an electronic communication system.

81. (previously presented) The kit of claim 74, wherein said electronic communication system transmits said data to a distant computer system for processing.

82. (previously presented) The kit of claim 72, wherein said instructions direct the fate of said data according to said subject's preference.

83. (previously presented) The kit of Claim 72, wherein said instructions comprise information to optimize perioperative care that, based on at least the presence of variant alleles of two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNF*α and *TNF*β, directs a user to a specific perioperative clinical pathway for said subject.

84. (previously presented) A kit for generating a perioperative genomic profile for a subject, comprising:

a) reagents configured such that when exposed to a sample containing

target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNF*α and *TNF*β so as to generate a genomic profile for use in selecting a perioperative course of action for said subject; and

b) a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents to indicate an anesthesia treatment course of action.

85. (previously presented) The kit of Claim 84, wherein said instructions indicate an a general anesthesia treatment course of action.

86. (previously presented) The kit of Claim 85, wherein said general anesthesia is an inhalational treatment course of action.

87. (previously presented) The kit of Claim 85, wherein said general anesthesia is an intravenous treatment course of action.

88. (previously presented) The kit of Claim 85, wherein said general anesthesia is a combined inhalational and intravenous treatment course of action.

89. (previously presented) The kit of Claim 84, wherein said instructions indicate an a regional anesthesia treatment course of action.

90. (previously presented) The kit of Claim 84, wherein said instructions indicate a combined regional and general treatment course of action.

91. (previously presented) The kit of Claim 84, wherein said instructions indicate an anesthesia treatment course of action during a medical procedure.

92. (previously presented) The kit of Claim 84, wherein said instructions indicate dosages of analgesic compounds.

93. (previously presented) The kit of Claim 84, wherein said instructions indicate increasing the dosage of analgesic compounds metabolized by CYP2D6.

94. (previously presented) The kit of Claim 84, wherein said instructions indicate decreasing the dosage of analgesic compounds metabolized by CYP2D6.

95. (previously presented) The kit of Claim 84, wherein said instructions indicate prophylaxis for thrombosis.

96. (previously presented) The kit of Claim 84, wherein said instructions indicate increasing prophylaxis for thrombosis mediated by variant alleles of *F5, F2, MTHFR, MTR, MTRR,* and *CBS.*

97. (previously presented) The kit of Claim 84, wherein said instructions indicate decreasing prophylaxis for thrombosis mediated by variant alleles of *F5, F2, MTHFR, MTR, MTRR,* and *CBS.*

98. (previously presented) The kit of Claim 84, wherein said instructions indicate monitoring procedures.

99. (previously presented) The kit of Claim 84, wherein said instructions indicate pre-operative phenotypic tests and consultations.

100. (previously presented) The kit of Claim 84, wherein said instructions provide a prognosis after an anesthesia treatment course of action.

101. (previously presented) A kit for generating a perioperative genomic profile for a subject, comprising:

a) reagents configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNF*α and *TNF*β so as to generate a genomic profile for use in selecting a perioperative course of action for said subject; and

b) a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents to indicate a surgical treatment course of action.

102. (previously presented) The kit of Claim 101, wherein said instructions indicate a non-invasive surgery treatment course of action.

103. (previously presented) The kit of Claim 101, wherein said instructions indicate an invasive surgery treatment course of action.

104. (previously presented) The kit of Claim 101, wherein said instructions provide a prognosis after a surgical treatment course of action.

105. (previously presented) The kit of Claim 101, wherein said instructions indicate a post-operative treatment course of action.

106. (previously presented) A perioperative genomic profile kit having component parts configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical

procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*, so as to generate a genomic profile for use in selecting a perioperative course of action for said subject and thereby providing a subject-specific clinical pathway for said subject, comprising information to optimize perioperative care that, based at least on the presence or absence of said variant alleles of two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ* measured by said kit, directs a user to a specific clinical pathway of medical intervention for said subject.

107. (previously presented) A perioperative genomic profile kit having component parts configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*, so as to generate a genomic profile for use in selecting a perioperative course of action for said subject and thereby providing a subject-specific clinical pathway for said subject, comprising information to optimize perioperative care that, based at least on the presence or absence of said variant alleles of two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ* measured by said kit, directs a user to a specific clinical pathway of anesthesia intervention for said subject.